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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,043	02/20/2002	Markus Kostrzewa	B0032/7019	5152

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EXAMINER
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ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/079,043	Kostrzewa
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 20, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-23* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. *10/079,043* .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. As a matter of fact, no steps are recited in the claim. The omitted steps are: a) providing a genomic DNA suspected of having mutation; b) selecting suitable primer having a photocleavable linker capable of mutation-dependent primer extension; c) amplifying the genomic DNA under suitable condition; d) cleaving the amplified DNA by UV light irradiation; and e) analyzing the cleaved DNA by mass spectrometry.

Claim 7 recites the limitation "the internucleotide cyanoethyl phosphite bond" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Objections

3. Claims 22-23 are objected to because of the following informalities: Claims 22-23 recites the word, "streptavidine". Appropriate correction is required.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of copending Application No. 10/079,271. Although the conflicting claims are not identical, they are not

patentably distinct from each other because claims 1-9 of copending Application No. 10/079,271 encompass the cleaving of the photocleavable linker by UV light radiation of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-6, 18, and 21-23 are rejected under 35 U.S.C. 102 (b) as being anticipated by Van Ness et al. (PCT International Publication Number WO 97/27325) (July 31, 1997).

Van Ness et al. teaches a method for mass spectrometric analysis of known mutation sites in genome DNA by mutation-dependent primer extension, wherein the nucleotide chain of the extension primer contains a photocleavable linker which is cleaved by UV light irradiation before mass spectrometric analysis (Page 64, line 25 to page 65, line 25, and Figure 13 and Example 2 on page 92 and Claims 17, 18, 21 and 25 and page 76, lines 12-21).

Van Ness et al. teaches a method, wherein the linker is located 3 to 10 bases from the 3' position of the primer (Figure 13).

Van Ness et al teaches a method, wherein the linker is derived from the class of chemical compounds known as o-nitro benzyl derivatives (page 35, all Figures and page 48, lines 17-26 including the Figure).

Van Ness et al teaches a method, wherein the extension is carried out by using a mixture of four types of nucleoside triphosphate derivative terminators so that extension only takes place by precisely one base (page 65, line 28 to page 68, line 13).

Van Ness et al teaches a method, wherein dideoxynucleoside triphosphates are used as the nucleoside triphosphate derivative terminators (page 61, lines 10-34 and page 87, lines 8-17).

Van Ness et al teaches a method, wherein the extension using a mixture of non-terminating and terminating nucleoside triphosphate derivatives is carried out so as to produce length differences in the extended primers of at least one base depending on mutation (page 68, lines 1-14).

Van Ness et al teaches a method, wherein ionization in the mass-spectrometric mass determination is achieved by using matrix-assisted laser desorption and ionization (Example 13).

Van Ness et al teaches a method, wherein the 5' position of the extension primer is biotinylated and can inherently be bonded to streptavidin molecules which may be fixed to a surface for the purpose of purging all the components of the reaction fluid which was required for the extension (Example 11).

Van Ness et al inherently teaches a method, wherein the streptavidin may be bonded to the surface of a sample support which is also used for further mass-spectrometric analysis (Example 11).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 7-17, and 19-20 are rejected under 35 U.S.C. 103(a) as being obvious over Van Ness et al. (PCT International Publication Number WO 97/27325) (July 31, 1997) in view of Gut

et al. (PCT International Publication Number WO 96/272681) (September 12, 1996) further in view of Sauer et al. (Nucleic Acids Research, (2000), Vol. 28 (5), pages e13 I-viii).

Van Ness et al teach the method of claims 1-6, 18, and 21-23 as described above including the chemical group carrying the charge is quaternary ammonium group (Page 49, lines 3-10 and page 56, lines 25-32).

Van Ness et al do not teach the method, wherein the internucleotide cyanoethyl phosphite bond of the primer nucleotides between the linker and the 3' position are sulphurized forming phosphorothioate nucleotides, and wherein the phosphorothioate nucleotides are alkylated before analysis by mass spectrometry.

Sauer et al. teach the method, wherein the internucleotide cyanoethyl phosphite bond of the primer nucleotides between the linker and the 3' position are sulphurized forming phosphorothioate nucleotides, and wherein the phosphorothioate nucleotides are alkylated before analysis by mass spectrometry (MATERIALS and METHODS Section, alkylation reaction and Figure 1).

Van Ness et al do not teach the method, wherein the alpha-thiodideoxynucleoside triphosphates are used as the nucleoside triphosphate derivative terminators.

Sauer et al. teach the method, wherein the alpha-thiodideoxynucleoside triphosphates are used as the nucleoside triphosphate derivative terminators (MATERIALS and METHODS Section, Primer extension reaction).

Van Ness et al do not teach the method, wherein the alpha-thionucleoside triphosphate derivative terminators carries a chemical group with a positive charge in addition located on the second, third or fourth nucleobase counting from the 3' position.

Sauer et al. teach the method, wherein the alpha-thionucleoside triphosphate derivative terminators carries a chemical group with a positive charge in addition located on the second, third or fourth nucleobase counting from the 3' position (MATERIALS and METHODS Section, first and second paragraph).

Van Ness et al do not teach the method, wherein the primer for the primer extension carries an anchor amino group before the analysis by mass spectrometry is carried out.

Sauer et al. teach the method, wherein the primer for the primer extension carries an anchor amino group before the analysis by mass spectrometry is carried out (MATERIALS and METHODS Section, first and second paragraph).

Van Ness et al do not teach the method, wherein a matrix alpha-cyano-4-hydroxycinnamic acid methyl ester is used which does not contribute to the transfer of charge to the DNA products being measured.

Sauer et al. teach the method, wherein a matrix alpha-cyano-4-hydroxycinnamic acid methyl ester is used which does not contribute to the transfer of charge to the DNA products being measured (MATERIALS and METHODS Section, Sample preparation for MALDI analysis subsection).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein a matrix alpha-cyano-4-hydroxycinnamic acid methyl ester is used which does not contribute to the transfer of charge to the DNA products being measured and specific chemically modified primers of Sauer et al. in the method of Van Ness et al., since Sauer et al. states, "The procedure is useful for high throughput genotyping as it is required for gene identification and pharmacogenomics where large number of DNA samples have to be analyzed (Abstract, page e13i, column 2, lines 3-6)." An ordinary practitioner would have been motivated to combine and substitute the method, wherein a matrix alpha-cyano-4-hydroxycinnamic acid methyl ester is used which does not contribute to the transfer of charge to the DNA products being measured and specific chemically modified primers of Sauer et al. in the method of Van Ness et al.. in order to achieve the express advantages noted by Sauer et al. of a procedure useful for high throughput genotyping as it is required for gene identification and pharmacogenomics where large number of DNA samples have to be analyzed.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, who can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Arun Chakrabarti
Patent Examiner
Art Unit 1634

Arun Kr. Chakrabarti
ARUN K. CHAKRABARTI
PATENT EXAMINER

April 4, 2003